

REMARKS

Status of the claims

Claims 1-3, 5-7, 9-12, 14-17, 21, 22, and 24-41 are pending in the application. By this amendment, claims 1, 10, 16, 17, 24, 25, 33, 34, and 38 are amended; and claims 35-37 are cancelled. Thus, following entry of this amendment, claims 1-3, 5-7, 9-12, 14-17, 21, 22, 24-34, 38-41 are pending.

As discussed during the telephone interview, claims 1, 16, 17, 24, 33, 34, and 38 have been streamlined and the limitations in the deleted step or steps are included in the next step that follows. Claims 1, 10, and 25 have been amended to include elements in claims 35-37. No new matter is added by this amendment.

With respect to all amendments and cancelled claims, Applicant has not dedicated or abandoned any unclaimed subject matter and moreover has not acquiesced to any rejections and/or objections made by the Patent Office. Applicant reserves the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional application.

Telephone interview

Applicant thanks the Examiner and Examiner Scott Priebe for extending the courtesy for a telephone interview on August 27, 2003, with Dr. Kim Clary and Applicant's representatives Catherine Polizzi and Jie Zhou, and for providing helpful suggestions, which are reflected in this response. The substance of the interview, during which issues in the Office Action were discussed, is reflected in this response. Claims and art discussed are as indicated in the Interview Summary. All objections and rejections raised in the Office Action were discussed, and the points presented are reflected in this response. In addition, proposed amendments to claims 1, 16, 17, 24, 33, 34, and 38 were discussed and the Examiners indicated that these amendments

would be acceptable. These amendments which are referred to above under "Status of the claims", are presented in this response.

Applicant's representative wishes to clarify one point from the Interview Summary and make a correction. In the context of discussing the 35 U.S.C. §112, first paragraph rejection, the issue of whether the p40 promoter could be replaced with a heterologous promoter and maintain the arrangement of rep and cap as in the AAV genome was discussed. Dr. Clary stated that AAV p40 promoter is in an intron of the rep gene. This statement was found to be incorrect after the interview. Applicant, Applicant's representatives, and Dr. Clary apologize for this error and wish to correct the record. Applicant's representatives also wish to provide clarification that neither Applicant's representatives nor Dr. Clary stated that "the term 'arranged as in the AAV genome' means that one skilled in the art can replace the promoter (p40) for cap located in an intron of the rep gene with a promoter and not disturb the overall arrangement of the rep and cap gene in the plasmid compared to an AAV genome." In view of the amendments to the claims to reciting p40 promoter is used for cap, however, any consequence of substituting a heterologous promoter for a p40 promoter with respect to arrangement in the AAV genome is moot.

Specification

The Examiner objected to the specification for informalities of ATCC accession no. missing on page 37, line 5 and incorrect address of ATCC on page 37, line 4. During the telephone interview, the Examiner pointed out that "ATCC" should be shown in the specification as trademark on pages 5, 35, and 37.

Applicant respectfully notes that the specification has been amended to include ATCC accession numbers missing on page 37, line 5, and the address of ATCC on page 37, line 4 has been corrected. Applicant also respectfully notes that the specification has been amended on pages 35 to show ATCC as trademark. However, Applicant cannot find ATCC used on page 5 and page 37 of specification and thus no correction has been made.

Rejections under 35 U.S.C. § 112, first paragraph

Applicant thanks the Examiner for withdrawal of enablement rejection of claims 1-17 and 21-23 under 35 USC §112 first paragraph.

Claims 1-3, 5-7, 9-12, 14-17, 21, 22, 24-34 and 38-41 are rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner contends that the claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner states that claims of this application read on operably linking an endogenous promoter or a heterologous promoter to the AAV cap gene in view of claims 35-37. The Examiner alleges that the specification provides sufficient description of an AAV cap gene operably linked to the AAV p40 promoter (the endogenous promoter of the cap gene), but does not provide sufficient description of a heterologous promoter operably linked to the AAV cap gene. The Examiner further alleges that the specification does not disclose a genus of endogenous or heterologous promoters that are operably linked to the cap gene.

Applicant respectfully traverses this rejection.

The MPEP states that “[t]here is a strong presumption that an adequate written description of the claimed invention is present when the application is filed”, and further states that “[t]o satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed the invention”: MPEP, §2163.I and §2163.I.A. In addition, the MPEP provides: “Generally, there is an inverse correlation between the level of skill and knowledge in the art and the specificity of disclosure necessary to satisfy the written description requirement. Information which is well known in the art need not be described in detail in the specification.” MPEP §2163.II.A.2 (emphasis added).

Applicant respectfully notes the specification of the instant application provides that “[i]n constructing packaging cell lines according to the present invention, the cells are provided with a

stably integrated AAV cap gene operably linked to a promoter, and a stably integrated AAV rep gene operably linked to a heterologous promoter." It is well known to one skilled in the art that "a promoter" can be an endogenous promoter or a heterologous promoter. As discussed during the telephone interview, since heterologous promoters are well known in the art, Applicant is not required to disclose heterologous promoters in detail in the specification. Given the "strong presumption that an adequate written description of the claimed invention is present when the application is filed" (MPEP §2163.I.A), Applicant respectfully submits that the claims are adequately described in accordance with 35 U.S.C. §112, ¶1.¹

However, in the interest of expediting prosecution and without acquiescence to the rejection, all claims as amended recite that AAV cap gene is operably linked to AAV p40 promoter. Thus, this rejection is moot. Applicant respectfully requests that the rejection be withdrawn.

Double Patenting

Claims 1, 2, 6, 10, 11, 12, 15, 16, 17, 21, 22, 24, 25, 26, 30, 32, 34 and 40 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 9, 11, 12, 15, 17, 18, and 21 of U.S. Patent No. 6,541,258. The Examiner contends that "'258 claims a mammalian cells and methods of generating a mammalian cell useful for high efficiency packaging of an rAAV vector comprising stably integrated an AAV rep gene operably linked to a promoter and an AAV cap gene operably linked to a promoter" and "the definition in the specification of '258 for a promoter operably linked to an AAV cap gene embraces a helper virus inducible heterologous promoter (column 22, lines 1-24)". The Examiner states that "although the conflicting claims are not identical, they are not patentably distinct from each other".

¹ Applicant respectfully notes that the issues in the two cases cited by the Examiner in the Office Action are related to enablement issues and are not applicable to the written description requirement.

Applicant respectfully traverses this rejection. A double patenting rejection relies on a comparison of the claims of the application at issue with the claims in the patent over which the application claims are rejected. *See* MPEP § 804. When the application at issue is a later-filed application, a one-way analysis of obviousness is needed, i.e., whether the invention defined in a claim in the application is an obvious variation of the invention defined in a claim in the patent. *See id.*; *see also In re Berg*, 46 USPQ2d 1226 (Fed. Cir. 1998). The analysis employed in an obviousness-type double patenting rejection parallels the guidelines or analysis of a 35 U.S.C. § 103 obviousness determination. *See* MPEP § 804. Applicant respectfully submits that a one-way analysis should not apply to the instant application, but rather a two-way test. However, even if one-way analysis is applicable, Applicant respectfully submits that the current claims are patentably distinct over claims 9, 11, 12, 15, 17, 18, and 21 of the '258 patent.

Applicant respectfully notes that claims 9, 11, 12, 15, 17, 18, and 21 of the '258 patent are directed to methods of generating mammalian cells and mammalian cells useful for high efficiency packaging of rAAV vectors. These claims all recite (in part) "an AAV split-cap gene, wherein said split-cap gene is uncoupled from Rep78-specific sequences of an AAV rep gene, wherein p40 promoter of said split-cap gene is replaced with a first heterologous promoter which is operably linked to said split-cap gene"; "an AAV rep78 gene, wherein said rep78 gene is uncoupled from Cap-specific sequences of an AAV cap gene, wherein p5 promoter of said rep78 gene is replaced with a second heterologous promoter which is operably linked to said rep78 gene"; and "an AAV rep52 gene, wherein said rep52 gene is uncoupled from Rep78-specific sequences of an AAV rep gene, wherein p19 of said rep52 gene is replaced with a third heterologous promoter which is operably linked to said rep52 gene". Accordingly, in these claims, the AAV split-cap gene is uncoupled from Rep78-specific sequences, rep78 gene is uncoupled from Cap-specific sequences, and rep52 gene is uncoupled from Rep78-specific sequences. In addition, all three promoters (p5, p19, and p40) are replaced with heterologous promoters.

In contrast, claims of the instant application as amended recite (in part) AAV cap gene is "operably linked to AAV p40 promoter" and "p5 promoter function has been replaced by the helper virus-inducible heterologous promoter". The p40 and the p19 promoter in the instant claims as amended are not replaced by a heterologous promoter. In addition, claims of the instant application recite (in part) that said mammalian cell is prepared by introducing "a single plasmid comprising AAV rep and AAV cap arranged as in the AAV genome" into the mammalian cell. Thus, claims in the instant application are patentably distinct over those claims of the '258 patent, and obviousness-type double patenting rejection may be properly withdrawn.

In view of the above, Applicant respectfully requests withdrawal of this rejection.

CONCLUSION

Applicant believes that the claims are in condition for allowance. Early notification to that effect is earnestly solicited. Should Examiner Whiteman find any issues outstanding after consideration of this Amendment, he is respectfully requested to contact the undersigned at (650) 813-5651.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicant petition for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 226272001403. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

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